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EXAMINER	
LIN, JERRY	

ART UNIT	PAPER NUMBER
1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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Office Action Summary	Application No.	Applicant(s)	
	10/022,249	VEGA ET AL.	
	Examiner	Art Unit	
	Jerry Lin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-10,12,14-33 and 42-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-10,12,14-33 and 42-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/2/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' arguments and amendments, filed November 22, 2006, have been fully considered and they are deemed to be persuasive in part. However, in light of the amendments, the following rejections are deemed necessary. The following rejections and/or objections are newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1-3, 5, 6, 8-10, 12, 14-21, 22, 23, 32 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blazquez et al. (Antimicrobioal, Agents, and Chemotherapy (Jan. 1995) Volume 39, Number 1, pages 145-149) in view of Giver et al. (PNAS (1998) Volume 95, pages 12809-12813).

The instant claims are drawn to a method of identifying proteins with different properties by producing separate sets of nucleic acid molecules, wherein each nucleic acid set is produced by changing one codon to a pre-selected codon, and each nucleic acid set encodes for a protein that different from the encoded proteins of other nucleic acid sets by one amino acid, and wherein all nucleic acid molecules in a set encode for the same modified protein; introducing each nucleic acid set into host cells on an array; expression the proteins; and screening the proteins for a chemical, physical, or biological property that differs from the target proteins; and designating proteins with a different property from the target protein as a hit.

Regarding claims 1, 2, 8, 22, and 23, Blazquez et al. teach a method wherein separate sets of nucleic acid molecules are produced, wherein all the nucleic acids in the set encode the same modified protein, wherein the nucleic acid molecules are produced by changing one codon in the target protein to a pre-selected codon, wherein each of the encoded proteins different each other by one amino acid (abstract; page 145, right column, under "Recombinant DNA techniques" – page 146, right column); individually introducing each set of nucleic acid molecules into host cells (page 145, right column, under "Recombinant DNA techniques" – page 146, right column); expressing the encoded proteins (page 146, right column); individually screening each

set of encoded proteins to determine if the proteins have a predetermined chemical physical or biological property that differs from the target protein such that each protein is a hit and each mutation is a hit position (page 146, right column bottom – 148, left column). Blazquez et al. also teach wherein the activity of the modified protein is at least 75% as compared to an unmodified target protein (page 146, left column– page 147, right column).

Although, Blazquez et al. teach creating separate cell extracts grown in separate mediums, Blazquez et al. does not teach wherein the host cells are organized in an addressable array.

Regarding claims 1, 3, 5, 6, 22, and 23, Giver et al. teach growing cells in an addressable array (96 well plates) (page 12810, left column top paragraph).

Regarding claim 9, 10, and 17-19, Giver et al. teach modifying the nucleic acids that encode modified hits and introducing these nucleic acids into cells and screening for a nucleic acid that encodes a protein with a predetermined property that differs from a target protein (page 12811, left column).

Regarding claim 12, Giver et al. teach using nucleic acid shuffling, recombination or random mutagenesis (page 12809, right column, bottom – page 12877, left column' page 12812, left column).

Regarding claims 14, 15, 43 and 44, Blazquez et al. teach wherein the preselected codons are codons that encode Ser or Lys (page 146, right column – page 146, left column).

Regarding claims 16 and 42, Giver et al. teach wherein the identified nucleic acid molecules are produced by systematically replacing each identified codon with another amino acid (page 12810, right column, bottom – page 12811, left column; page 12812, left column).

It would have been obvious for one of ordinary skill in the art at the time of the invention to modify the method of Blazquez et al. with Giver et al. to gain the benefit of being able to test for several proteins as once by using an addressable array as well as the benefit of further modifying target protein variants for further analysis. The use of addressable arrays is a well-known method in the art in order to study several compounds at once. Giver et al. teach that will one array plate, they were able to assay several variants of a protein at once (page 12810, left column). Given these time savings, one of ordinary skill in the art would be motivated to used an addressable array in order to test for several compounds, such as the seven mutations and target protein in Blazquez et al.'s method, to gain efficiency in their experiments. Giver et al. also teach that further modifying target protein variants can lead to compounds with more desirable properties (page 12811, left column). Thus, one of ordinary skill in the art would be motivated to modify the compounds made by Blazquez et al. using Giver et al.'s method in order to obtain compounds with more desirable properties.

4. Regarding claims 32 and 33, according to the MPEP Section 2144.04, Part III, "providing an automatic or mechanical means to replace a manual activity which accomplished the same result is not sufficient to distinguish over the prior art" *In re Venner, 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958).*" Claims 32 and 33 are

merely computer automations of claim 1. Thus, it would be obvious to one skilled in the art to use a computer to automate the known processes disclosed by Blazquez et al. and Giver et al.

Note:

5. Applicants responded to the previous rejection made under 35 U.S.C. §102 under Giver et al. as defining addressably arrayed as, "As described in the specification addressably arrayed means that the identity of the cells by virtue of the protein expressed is known." However, the Specification appears to contradict this definition. The Specification states on page 27, "An addressable array is one in which the member of the array are identifiable, typically by position on a solid phase support or by virtue of an identifiable or detectable label . . . ." A 96 well plate is within the scope of this definition, because the row and column number of each well (i.e, position of each well) may be used to identify what one of ordinary skill in the art has placed in the well. This office action will use the definition provided in the Specification.

6. Claims 7, 24, and 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blazquez et al. (Antimicrobioal, Agents, and Chemotherapy (Jan. 1995) Volume 39, Number 1, pages 145-149) in view of Giver et al. (PNAS (1998) Volume 95, pages 12809-12813) as applied to claim 1 above, and further in view of Berlioz et al. (US 5,925,565).

The instant claims are drawn to a method of identifying proteins with different properties by producing separate sets of nucleic acid molecules, wherein each nucleic acid set is produced by changing one codon to a pre-selected codon, and each nucleic acid set encodes for a protein that different from the encoded proteins of other nucleic acid sets by one amino acid, and wherein all nucleic acid molecules in a set encode for the same modified protein; introducing each nucleic acid set into host cells on an array; expression the proteins; and screening the proteins for a chemical, physical, or biological property that differs from the target proteins; and designating proteins with a different property from the target protein as a hit. In particular, the instant claims include using eukaryotic cells or assessing the titer of viral vectors.

Blazquez et al. and Giver et al. are applied as above.

However, Blazquez et al. and Giver et al. do not teach using eukaryotic cells or assessing the titer of the viral vectors.

Berlioz et al. teach assessing the titer of viral vectors after transfection for each set of eukaryotic cells (column 14, lines 39-65), and where the viral vector encodes for a protein involved in viral replication (column 5, lines 35-65).

It would have been obvious at the time of the invention to modify the methods taught by Blazquez et al. and Giver et al. with Berlioz et al. in order to study the effects of the protein in an eukaryotic setting. Berlioz et al. teaches a method that allows an eukaryotic cells, such as a human cell, to express a desired protein (column 6, lines 5-22) for the purpose of producing a therapeutic treatment (column 7, lines 15-25). Giver et al.'s and Blazquez et al.'s methods teaches screening for different proteins that

exhibit a desired biological, chemical, or physical property. Thus one of ordinary skill in the art seeking to create a new therapeutic treatment, would be motivated to use Giver et al. and Blazquez et al.'s methods to design a product and use Berlioz et al.'s method to express the protein in an eukaryotic cell.

7. Claim 25 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blazquez et al. (Antimicrobioal, Agents, and Chemotherapy (Jan. 1995) Volume 39, Number 1, pages 145-149) in view of Giver et al. (PNAS (1998) Volume 95, pages 12809-12813) in view of Berlioz et al. (US 5,925,565) as applied to claim 24 above, and further in view of Rivet et al. (Gene Therapy (2000) Volume 7, pages 924-929).

The instant claims are drawn to a method of identifying proteins with different properties by producing separate sets of nucleic acid molecules, wherein each nucleic acid set is produced by changing one codon to a pre-selected codon, and each nucleic acid set encodes for a protein that different from the encoded proteins of other nucleic acid sets by one amino acid, and wherein all nucleic acid molecules in a set encode for the same modified protein; introducing each nucleic acid set into host cells on an array; expression the proteins; and screening the proteins for a chemical, physical, or biological property that differs from the target proteins; and designating proteins with a different property from the target protein as a hit. In particular, the instant claims are drawn to a method of determining the titer using real time virus titer and tagged replication and expression enhancement.

Blazquez et al., Giver et al., and Berlioz et al. are applied as above.

However, Blazquez et al., Giver et al., and Berlioz et al. do not teach real-time virus titering or tagged replication and expression enhancement.

Regarding claims 25 and 26, Rivet et al. teaches real time virus titering (page 925) and using tagged replication and expression enhancement (page 926, right column).

It would have been obvious for one of ordinary skill in the art to modify the methods of Blazquez et al., Giver et al., and Berlioz et al. with Rivet et al. to gain the benefit of determining the effectiveness of viral vectors. Berlioz et al. teach that one of his goals is to create an effective and stable viral vector (column 1, lines 10-17). Part of their method requires that they assess the titer of the viral vectors after transmission. Revet et al.'s method provides further insight into the stability and efficacy of the vector by offering real time titering. Thus one of ordinary skill in the art would be motivated to combine the methods of Blazquez et al., Giver et al., and Berlioz et al. with Rivet et al. in order to gain the benefit of assessing the stability and efficacy of viral vectors.

8. Claims 30 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blazquez et al. (Antimicrobioal, Agents, and Chemotherapy (Jan. 1995) Volume 39, Number 1, pages 145-149) in view of Giver et al. (PNAS (1998) Volume 95, pages 12809-12813) as applied to claim 1 above, and further in view of Persson et al. (Journal of Virology (1985) Volume 54, pages 92-97).

The instant claims are drawn to a method of identifying proteins with different properties by producing separate sets of nucleic acid molecules, wherein each

nucleic acid set is produced by changing one codon to a pre-selected codon, and each nucleic acid set encodes for a protein that different from the encoded proteins of other nucleic acid sets by one amino acid, and wherein all nucleic acid molecules in a set encode for the same modified protein; introducing each nucleic acid set into host cells on an array; expression the proteins; and screening the proteins for a chemical, physical, or biological property that differs from the target proteins; and designating proteins with a different property from the target protein as a hit. In particular, the instant claims use Hill analysis.

Blazquez et al. and Giver et al. are applied as above.

However, Blazquez et al. and Giver et al. do not teach using Hill analysis.

Persson et al. teach a method that uses the Hilll analysis for determining the rate in which hose cell are infected with viruses (abstract, page 94, left column).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Giver et al. and Blazquez et al. with the method of Persson et al. to gain the benefit of determining if the plasmids or vectors are infecting the host cells. Giver et al. and Blazquez et al. teaches creating host cells with desired nucleic acids. In such a method, it would be desirable to determine the rate of infection in order to determine how to structure and experiment (e.g., incubation times, concentration, etc.). Persson et al. provide a method of determining the rate of infection. Thus one of ordinary skill in the art would be motivated to combine the methods of Giver et al. and Blazquez et al. with the method of Persson et al. to gain the benefit of determining ther ate of infection of host cells to structure his experiments.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jerry Lin whose telephone number is (571) 272-2561. The examiner can normally be reached on 10:00-6:30, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JL

John S. Brusca 4 May 2007

JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER